PATENT
Docket No. 220002057202
Client Ref. No. 1995-091-4

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Wolfgang H. DILLMANN et al.

Serial No.: 09/664,127

Filing Date: September 18, 2000

For: GENE THERAPY FOR MYOCARDIAL ISCHEMIA

Examiner: S. Chen

Group Art Unit: 1633

DECLARATION OF DR. WOLFGANG H. DILLMANN PURSUANT TO 37 C.F.R § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Dr. Wolfgang H. Dillmann, declare as follows:

1. I am currently a Professor of Medicine at the University of California at San Diego. I am an expert in the area of Endocrinology and pathophysiological basis of cardiovascular disease. A current copy of my Curriculum Vitae is attached hereto as Exhibit 1.

2. I currently reside at 355 S. Nardo Avenue, Solana Beach, California 92075.

3. I am a co-inventor of the claims of the above-identified patent application. I have reviewed the pending claims. I have also read the Office Action dated January 31, 2002.

4. Results obtained from my laboratory demonstrate that administration of heat shock protein 70i (HSP70i) from an adenoviral vector administered to mouse myocardium *in vivo* protect against ischemic injury.

5. The experiments are described in the following paragraphs. Normal mice (25-30 g) were anesthetized with ketamine/xylasine and placed on a ventilator. A sternotomy was performed at the level of the 2nd intercostal space to gain access to the thoracic cavity. The heart

was exposed and an open stitch of 8-O Ethalon nylon suture was placed at the ap x of the left ventricle to allow the heart to be manipulated.

6. Starting at the apex and moving toward the base, five 10 µl (50 µl total) aliquots of adenovirus (10^{10} pfu) containing either an empty expression vector (SR-) or HSP70i were injected into the left ventricular free wall using a 0.5 ml insulin syringe with a fixed 29 gauge needle. The adenovirus comprising nucleic acid encoding HSP70i operably linked to the CMV promoter lacked the E1 gene and was replication-deficient. The control adenovirus lacked nucleic acid encoding HSP70i operably linked to the CMV promoter. After injections, the Ethalon suture was removed and the heart repositioned back into the chest cavity. The chest cavity was sutured closed, and a pneumothorax was prevented by using a chest tube to evacuate the air. The animals were removed from the ventilator and allowed to recover for 4 days.

7. At the end of 4 days the animals were sacrificed with an overdose of pentobarbital (10 mg/mouse). Hearts were excised and mounted on a Langendorff perfusion apparatus. A balloon was inserted into the left ventricle through the pulmonary vein and inflated to an end-diastolic pressure of 10 mmHg. The hearts were paced at approximately 400 bpm and the subsequent pressure development recorded using a 2 ft Millar pressure transducer and a computerized data acquisition system. Each heart underwent the following perfusion protocol: 15 minutes aerobic perfusion followed by 20 minutes of global no-flow ischemia, followed by 120 minutes of reperfusion. Function (dP/dt, pressure development) was assessed at the end of the initial 15 min aerobic perfusion and the end of 120 minutes of reperfusion.

8. In mice injected with adenoviral vectors expressing HSP70i, there was a significant improvement (p = less than 0.05) in the maximally developed systolic pressure dP/dt min; the decrease in diastolic pressure dP/dt minutes; and developed pressure. In contrast, no difference in contractile performance was observed in the ischemic hearts before the ischemic periods or in hearts injected with adenoviral vectors not expressing a HSP70i.

9. These results demonstrate that under *in vivo* conditions, increased expression of HSP70i from an adenoviral vector leads to significant protection against ischemic injury as determined by an improvement in contractile performance.

10. Results from additional experiments in the same animal model demonstrated that the release of creatine kinase, which is an indicator of ischemic injury after myocardial infarct in

humans, was significantly decreased in the mouse hearts injected with the adenovirus expressing HSP70i.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

7-3 2002
Date

W. Dillmann
Dr. Wolfgang H. DILLMANN

CURRICULUM VITAE

WOLFGANG H. DILLMANN,M.D.
Professor of Medicine

DATE OF BIRTH: December 8, 1939, Recklinghausen, Germany

PROFESSIONAL ADDRESS: University of California, San Diego
9500 Gilman Drive (BSB/5063)
La Jolla, CA 92093-0618
(858) 534-9934/534-9932, FAX

PERSONAL DATA: Married, Luise Steeger
Children, Thomas,Katja, Susanne, Christina

EDUCATION AND TRAINING:

1960	Baccalaureate, Gymnasium, Aschaffenburg, Germany
1968	University of Munich, School of Medicine, Germany, Examination in Medicine, Rotating Internship.
1970	M.D., University of Munich, Thesis: Renal Perfusion and Clearance Using Isotope Techniques.
1970 - 1971	Medical Internship, City Hospital Center, Elmhurst, Mt. Sinai Hospital, New York City.
1971 - 1972	Resident, Montefiore Hospital, Albert Einstein College of Medicine, New York.
1972 - 1975	Fellowship Endocrinology and Metabolism, Montefiore Hospital, Albert Einstein College of Medicine, New York.

PROFESSIONAL APPOINTMENTS:

1975 - 1976	Assistant Professor of Medicine Albert Einstein College of Medicine Bronx, New York
1976 - 1978	Assistant Professor of Medicine University of Minnesota
1979 - 1981	Assistant Professor of Medicine University of California, San Diego

1981 - 1987	Associate of Professor of Medicine University of California, San Diego
1987 - PRESENT	Professor of Medicine University of California, San Diego

PROFESSIONAL LICENSURE AND CERTIFICATION:

1972	American Board of Internal Medicine
1975	New York, Licensure
1976	Minnesota, Licensure
1977	American Board of Endocrinology and Metabolism
1979	California, Licensure

PROFESSIONAL SOCIETIES:

American Thyroid Association; Endocrine Society; American Diabetes Association; Western Society for Clinical Investigation; American Heart Association - Basic Science; American Federation for Clinical Research; American Society for Clinical Investigation; European Thyroid Association; Phi Beta Delta; American Society for Biochemistry & Molecular Biology; Deutsche Gesellschaft fur Endokrinologie; International Society for Heart Research, American Section, Assoc. of American Physicians, Heart Failure Society of America.

RESEARCH SUPPORT:

National Institute of Health
Merit Award, P.I. W. Dillmann
CARDIAC ISCHEMIA AND HSP's

National Institute of Health
R01, P.I. W. Dillmann
THYROID HORMONE ACTION IN THE HEART

National Institute of Health
R01, P.I. W. Dillmann
CARDIAC HYPERTROPHY AND SERCA2 GENE EXPRESSION

National Institute of Health
R01, P.I. W. Dillmann
DIABETIC CARDIOMYOPATHY AND CALCIUM FLUX

BIBLIOGRAPHY

I. ORIGINAL ARTICLES:

Surks MI, Koerner D, Dillmann WH, Oppenheimer JH. Limited capacity binding sites for L-triiodothyronine in rat liver nuclei. J Biol Chem 1973 248:7066-7072

Oppenheimer JH, Schwartz HL, Dillmann WH, Surks MI. Effect of thyroid hormone analogues on the displacement of [^{125}I]-triiodothyronine from hepatic and heart nuclei *in vivo*: Possible relationship to hormonal activity. Biochem Biophys Res Commun 1973 55:544-550

Dillmann WH, Surks MI, Oppenheimer JH. Quantitative aspects of iodothyronine binding by cytosol proteins of rat liver and kidney. Endocrinology 1974 96:492-498

Goslings B, Schwartz HL, Dillmann WH, Surks MI, Oppenheimer JH. Comparison of the metabolism and distribution of L-triiodothyronine and triiodothyroacetic acid in the rat: A possible explanation of differential hormone potency. Endocrinology 1976 98:666-675

Dillmann WH, Schwartz HL, Silva E, Surks MI, Oppenheimer JH. Effect of α-amanitin on the induction of hepatic enzymes by triiodothyronine. Proc 7th Int Thyroid Conf Boston, 1975 Excerpta Medica, International Congress Series No 1976 387:326-330

Oppenheimer JH, Schwartz HL, Surks MI, Koerner DH, Dillmann WH. Initiation of thyroid hormone action. Rec Prog Horm Res 1976 32:529-565

Dillmann WH, Silva E, Surks MI, Oppenheimer JH. Studies of a thyroid hormone and androgen dependent protein in rat liver cytosol. Acta Endocrinologia 1977 84:548-558

Dillmann WH, Schwartz HL, Silva E, Surks MI, Oppenheimer JH. α-amanitin administration results in a temporary inhibition of hepatic enzyme induction by triiodothyronine: Further evidence favoring a long-lived mediator of thyroid hormone action. Endocrinology 1977 100:1621-1627

Dillmann WH, Mendecki J, Koerner D, Schwartz HL, Oppenheimer JH. Triiodothyronine (T_3) stimulated formation of poly(A)-containing nuclear RNA and mRNA in rat liver. Endocrinology 1978 102:568-575

Dillmann WH, Schwartz HL, Oppenheimer JH. Selective alterations in hepatic enzyme response after reduction of nuclear triiodothyronine receptor sites by partial hepatectomy and starvation. Biochem Biophys Res Common 1978 80:259

Dillmann WH, Bonner RA, Oppenheimer JH. Glucagon administration decreases hepatic nuclear triiodothyronine binding capacity. Endocrinology 1978 102:1633-1636

Mendecki J, Dillmann WH, Wolley RC, Oppenheimer JH, Koss LG. Effect of thyroid hormone on the ploidy of rat liver nuclei as determined by flow-cytometry. Proc Soc Exp Biol Med 1978 158:63-67

Towle HC, Dillmann WH, Oppenheimer JH. Messenger RNA content and complexity of euthyroid and hypothyroid rat liver. J Biol Chem 1979 254:2250-2257

Dillmann WH, Oppenheimer JH. Glucagon influences the expression of thyroid hormone action: Discrepancy between nuclear T_3 receptor number and enzyme response. Endocrinology 1979 105:74-79

Bantle JP, Dillmann WH, Oppenheimer JH, Bingham Ch, Runger GC. Common clinical indices of thyroid hormone action: Relationship to serum-free 3, 5, 3'-triiodothyronine concentration and estimated nuclear occupancy. J Clin Endocrinol Metabol 1980 50:286-293

Dillmann WH. Diabetes mellitus induces change in cardiac myosin of the rat. Diabetes 1980 29:579-582

Dillmann WH. Influence of thyroid hormone administration of myosin ATPase activity and myosin isoenzyme distribution in the heart of diabetic rats. Metabolism 1982 31:199-204

Dillmann WH, Berry S, Alexander NM. A physiological dose of triiodothyronine normalizes cardiac myosin ATPase activity and changes myosin isoenzyme distribution in semi-starved rats. Endocrinology 1983 112:2081-2087

Dillmann WH, Barrieux A, Neeley WE, Contreras P. Influence of thyroid hormone on the *in vitro* translational activity of specific mRNA's in the rat heart. J Biol Chem 1983 258:7738-7745

Sogol PB, Hershman JM, Reed AW, Dillmann WH. The effects of amiodarone on serum thyroid hormones and hepatic thyroxine 5'-monodiodination in rats. Endocrinology 1983 113:1464-1469

Dillmann WH, Barrieux A, Reese GS. Effect of diabetes and hypothyroidism on the predominance of cardiac myosin heavy chains synthesized *in vivo* or in a cell-free system. J Biol Chem 1984 259:2035-2038

Dillmann WH. Fructose feeding increases Ca^{++}-activated myosin ATPase activity and changes myosin isoenzyme distribution in the diabetic rat heart. Endocrinology 1984 114:1678-1685

Dillmann WH. Methyl palmoxirate increases Ca^{++}-activated myosin ATPase activity and changes myosin isoenzyme distribution in the diabetic rat heart. Am J Physiol 1985 248:E602-E606

Dillmann WH. Myosin isoenzyme distribution and Ca^{++}-activated ATPase activity in the rat heart is influenced by fructose feeding and triiodothyronine. Endocrinology 1985 116:2160-2166

Barrieux A, Neeley WE, Dillmann WH. Diabetes-induced alterations in the translational activity of specific messenger ribonucleic acids from rat hearts. Circ Res 1985 57:296-303

Shanker R, Neeley WE, Dillmann WH. Rapid effects of insulin on the *in vitro* translational activity of specific mRNA's in the diabetic rat heart. Am J Physiol 1986 250:E558-E563

Dillmann WH, Mehta HB, Barrieux A, Guth BD, Neeley WE, Ross J, Jr. Ischemia of the dog heart induces the appearance of a cardiac mRNA coding for a protein with migration characteristics similar to heat shock/stress protein 71. Circ Res 1986 59:110-114

Shanker MR, Neeley WE, Dillmann WH. Time course of response of individual messenger RNAs in the rat heart to T_3. J Mol Cell Cardiol 1987 19:595-601

Cagliero E, Barrieux A, Lehman C, Dillmann WH. Diabetes-induced changes of proteins synthesized by adult cardiac myocytes are partially reversed by insulin. J Mol Cell Cardiol 1988 20:427-434

Rohrer D, Dillmann WH. Thyroid hormone markedly increases the mRNA coding for sarcoplasmic reticulum Ca^{++} ATPase in the rat heart. J Biol Chem 1988 263:6941-6944

Boheler KR, Dillmann WH. Cardiac response to pressure overload in the rat: Selective alterations of translational products. Circ Res 1988 63:448-456

Mehta HB, Popovich B, Dillmann WH. Ischemia induced changes in the level of mRNAs coding for stress protein 71 and creatine kinase M. Cir. Res 1988 63:512-517

Popovich BK, Boheler KR, Dillmann WH. Diabetes decreases creatine kinase enzyme activity and mRNA level in the rat heart. Amer J Physiol 1989 257:E573-E577

Dillmann WH, Barrieux A, Shanker R. Influence of thyroid hormone on myosin heavy chain mRNA and other messenger RNAs in the rat heart. Endocrine Research 1989 15:565-577

Maciel LMZ, Polikar R, Rohrer D, Popovich BK, Dillmann WH. Age induced decreases in the mRNA coding for the sarcoplasmic reticulum Ca^{2+} ATPase of the rat heart. Cir Res 1990 67:230-234

Rohrer DK, Hartong R, Dillmann WH. Influence of thyroid hormone and retinoic acid on slow sarcoplasmic reticulum Ca^{++} ATPase and myosin heavy chain alpha gene expression in cardiac myocytes: delineation of cis-active DNA elements that confer responsiveness to thyroid hormone but not to retinoic acid. J Biol Chem 1991 266:8638-8646

Popovich BK, Sayen MR, Dillmann WH. Insulin responsiveness of CK-M and CK-B mRNA in the diabetic rat heart. Amer J Physiol 1991 261:E377-E381

Yuasa R, Eggo MC, Meinkoth J, Dillmann WH, Burrow GN. Iodide induces transforming growth factor beta 1 (TGF-β1) mRNA in sheep thyroid cells. Thyroid 1992 2:141-145

Su C-Y, Payne M, Strauss AW, Dillmann, WH. Selective reduction of creatine kinase subunit mRNAs in striated muscle of diabetic rats. Am J Physiol 1992 263:E310-E316

Villarreal FJ, Dillmann WH. Cardiac hypertrophy-induced changes in mRNA levels for TGF-β1, fibronectin, and collagen. Amer J Physiol 1992 266:H1861 - H1866

Sayen MR, Rohrer DK, Dillmann WH. Thyroid hormone response of slow and fast sarcoplasmic reticulum Ca^{2+} ATPase mRNA in striated muscle. Mol Cell Endocrinol 1992 87:87-93

Bouvet M, Feldman JI, Gill GN, Dillmann WH, Nahum AM, Russack V, Robbins KT. Surgical management of the thyroid nodule: Patient selection based on the results of fine needle aspiration cytology. Laryngoscope 1992 102:1353-1356

Iwaki K, Dillmann WH, Mestril R. Induction of HSP70 in cultured rat neonatal myocytes by hypoxia and metabolic stress. Circulation 1993 87:2023-2032

Villarreal FJ, Kim NN, Ungab GD, Printz MP, Dillmann WH. Identification of functional angiotension II receptors on rat cardiac fibroblasts. Circulation 1993 88:2849-2861

Mestril R, Chi S-H, Sayen MR, Dillmann WH. Isolation of a novel inducible rat heat shock protein (HSP70) gene and its expression during ischemia/hypoxia and heat shock. Biochem J 1994 298:561-569

Mestril R, Chi S-H, Sayen MR, O'Reilly K, Dillmann WH. Expression of inducible stress protein 70 in rat heart myogenic cells confers protection against simulated ischemia-induced injury. J Clin Invest 1994 93(2):759-767

Hartong R, Wang N, Kurokawa R, Lazar MA, Glass CK, Apriletti JW, Dillmann WH. Delineation of three different thyroid hormone response elements in the promoter of the rat sarcoplasmic reticulum Ca^{2+} ATPase gene: Demonstration that the retinoid X receptor binds 5' to the thyroid hormone receptor in response element 1. J Biol Chem 1994 269:13021-13029

Villarreal FJ, MacKenna DA, Omens JH, Dillmann WH. Myocardial remodeling in hypertensive REN-2 transgenic rats. Hypertension J 1995 25:98-104

Marber MS, Mestril R, Chi S-H, Sayen MR, Yellon DM, Dillmann WH. Overexpression of the rat inducible 70 kiloDalton heat stress protein in a transgenic mouse increases the resistance of the heart to ischemic injury. J Clin Invest 1995 95:1446-1456

Kim NN, Villarreal FJ, Printz MP, Lee AA, Dillmann WH. Tropic effects of angiotensin II on neonatal rat cardiac myocytes are mediated by cardiac fibroblasts. Am J Physiol 1995 269:E426-E437

Lee AA, Dillmann WH, McCulloch AD, Villarreal FJ. Angiotensin II stimulates the autocrine production of transforming growth factor-β1 in adult rat cardiac fibroblasts. J Mol Cell Cardiol 1995 27:2347-2357

Villarreal FJ, Lee AA, Dillmann WH, Giordano FJ. Adenovirus-mediated overexpression of human transforming growth factor-β1 in rat cardiac fibroblasts, myocytes and smooth muscle cells. J Mol Cell Cardiol 1996 28:735-742

Giordano FJ, Ping P, McKirnan MD, Nozaki S, DeMaria AN, Dillmann WH, Mathieu-Costello O, Hammond HK. Intracoronary gene transfer of fibroblast growth factor-5 increases blood flow and contractile function in an ischemic region of the heart. Nature Medicine 1996 2:534-539

Hutter JJ, Mestril R, Tam EKW, Sievers RE, Dillmann WH, Wolfe CL. Overexpression of inducible heat shock protein 72 in transgenic mice decreases infarct size *in vivo*. Circulation 1996 94:1408-1411

Hartong R, Villarreal FJ, Giordano F, Hilal-Dandan R, McDonough PM, Dillmann WH. Phorbol myristate acetate induced hypertrophy of neonatal rat cardiac myocytes is associated with decreased sarcoplasmic reticulum Ca^{2+} ATPase (SERCA2) gene expression and calcium reuptake. J Mol Cell Cardiol 1996 28:2467-2477

Mestril R, Giordano FJ, Conde AG, Dillmann WH. Adenovirus-mediated gene transfer of a heat shock protein 70 (hsp70i) protects against simulated ischemia. J Mol Cell Cardiol 1996 28:2351-2358

Moriscot AS, Sayen MR, Hartong R, Wu P, Dillmann WH. Transcription of the rat sarcoplasmic reticulum Ca^{2+} ATPase is increased by T_3 receptor isoform-specific interactions with the myocyte specific enhancer factor-2a. Endocrinology 1997 138:26-32

Wu PSC, Knowlton KU, Dillmann WH. α1-adrenergic stimulation inhibits T_3 induced expression of the rat heart sarcoplasmic reticulum Ca^{2+} ATPase gene. Endocrinology 1997 138:114-120

Piotrowicz R, Martin J, Dillmann WH, Levin E. HSP27 facilitates b-FGF release from endothelial cells. J Biol Chem 1997 272:7042-7047

He H, Giordano FJ, Hilal-Dandan R, Rockman HA, McDonough PM, Sayen MR, Swanson E, Dillmann WH. Overexpression of the rat sarcoplasmic reticulum (SR) Ca^{2+} ATPase gene in the heart of transgenic mice accelerates calcium transients and cardiac relaxation. J Clin Invest 1997 100:380-389

Giordano FJ, He H, McDonough P, Meyer M, Sayen MR, Dillmann WH. Adenovirus-mediated gene transfer reconstitutes depressed sarcoplasmic reticulum Ca^{2+} ATPase levels and shortens prolonged cardiac myocyte Ca^{2+} transients. Circulation 1997 96:400-403

Conde A, Lau SS, Dillmann WH, Mestril R. Induction of heat shock proteins by tyrosine kinase inhibitors in rat cardiomyocytes and myogenic cells confers protection against simulated ischemia. J Mol Cell Cardiol 1997 26:1927-1938

Martin JL, Mestril R, Hilal-Dandan R, Brunton LL, Dillmann WH. Small heat shock proteins and protection against ischemic injury in cardiac myocytes. Circulation 1997 96:4343-4348

Trost SU, Omens JH, Karlon WJ, Meyer M, Mestril R, Covell JW, Dillmann WH. Protection against myocardial dysfunction after a brief ischemic period in transgenic mice expressing inducible HSP70. J Clin Invest 1998 101:855-862

Su C-Y, Chong K-Y, Dillmann WH, Chang C, Owen UE, Lai C-C. Constitutive and inducible HSP70's are involved in oxidative resistance evoked by heat shock or ethanol. J Mol Cell Cardiol 1998 3:587-598

Ho PD, Zechner DK, He H, Dillmann WH, Glembotzki CC, McDonough PM. The Raf-MEK-ERK Cascade represents a common pathway for alteration of intracellular calcium by ras and protein kinase C in cardiac myocytes. J Bio Chem 1998 273(34):21730-21735

Bluhm W, Martin JL, Mestril R, Dillmann WH. Specific heat shock proteins protect microtubules during simulated ischemia in cardiac myocytes. Am J Physiol 275 (Heart Circ Physiol 44): H2243-H2249 1998

Tian R, Halow JM, Meyer M, Dillmann WH, Figueredo VM, Ingwall JS, Camacho SA. Thermodynamic limitation for Ca^{2+} handling contributes to decreased contractile reserve in rat hearts. Am J Physiol 275 (Heart Circ Physiol 44): H2064-H2071 1998

Meyer M, Dillmann WH. Sarcoplasmic reticulum Ca(2+)-ATPase overexpression by adenovirus mediated gene transfer and in transgenic mice. Cardiovascular Research 1998 37(2):360-366

Yao A, Zhi S, Dillmann WH, Barry WH. Sarcoplasmic Reticulum Function in Murine Ventricular Myocytes Overexpressing SR CaATPase. J Mol Cell Cardiol 30: 2711-2718, 1998

Mierkes PE, Cornel LM, Wilson KL, Dillmann WH. Heat Shock Protein 70 (Hsp70) protects post implantation murine embryos from the embryo lethal effects of hyperthermia. Developmental Dynamics 214:159-170, 1999.

Meyer M, Bluhm WF, He H, Post SR, Giordano FJ, Lew WY, Dillmann WH. Phospholamban-to-SERCA2 ratio controls the force-frequency relationship. Am J Physiol 1999 276:H779-H785

Martin JL, Hickey E, Weber LA, Dillmann WH, Mestril R. Influence of phosphorylation and oligomerization on the protective role of the small heat shock protein 27 in rat adult cardiomyocytes. Gene Expr 1999 7:349-355

He H, Meyer M, Martin JL, McDonough PM, Ho P, Lou X, Lew WY, Hilal-Dandan R, Dillmann WH. Effects of mutant and antisense RNA of phospholamban on SR Ca(2+)-ATPase activity and cardiac myocyte contractility. Circulation 1999 100:974-980

Bluhm, WF; Meyer, M; Sayen, MR; Swanson, EA; Dillmann, WH. Overexpression of sarcoplasmic reticulum Ca(2+)-ATPase improves cardiac contractile function in hypothyroid mice. Cardiovascular Research 1999 43(2):382-8

Lewis, SE; Mannion, RJ; White, FA; Coggeshall, RE; Beggs, S; Costigan, M; Martin, JL; Dillmann, WH; Woolf, CJ. A role for HSP27 in sensory neuron survival. Journal of Neuroscience 1999 19:8945-53

Gloss B, Sayen MR, Trost, SU, Bluhm WF, Meyer M, Swanson EA, Usala SJ, Dillmann WH. Altered cardiac phenotype in transgenic mice carrying the Δ337 threonine thyroid hormone receptor β mutant derived from the S family. Endocrinology 1999 140(3) 897-902

Bluhm WF, Kranias EG, Dillmann WH, Meyer M. Phospholamban: a major determinant of the cardiac force-frequency relationship. Am J Physiol Heart Circ Physiol 2000 278:H249-H255

Rajdev S, Hara K, Kokubo Y, Mestril R, Dillmann WH, Weinstein PR, Sharp FR. Mice overexpressing rat heat shock protein 70 are protected against cerebral infarction. Annals of Neurology 2000 47(6):782-91

Brewis N, Ohst K, Fields K, Rapacciuolo A, Chou D, Bloor C, Dillmann W. Dilated cardiomyopathy in transgenic mice expressing a mutant A subunit of protein phosphatase 2A.Am J Physiol Heart Cir Physiol 2000 279: H1307-H1318

Villegas S, Villarreal FJ, Dillmann WH. Leukemia inhibitory Factor and Interleukin-6 downregulate sarcoplasmic reticulum Ca2+ ATPase (SERCA2) in cardiac myocytes. Basic Research in Cardiology 2000 95(1):47-54

Gloss B, Villegas S, Villarreal FJ, Moriscot A, Dillmann WH. Thyroid hormone-induced stimulation of the sarcoplasmic reticulum Ca(2+) ATPase gene is inhibited by LIF and IL-6. Am J Physiol Endocrinol Metab 2000 278(4):E738-43

Trost SU, Swanson E, Gloss B, Wang-Iverson DB, Zhang H, Volodarsky T, Grover GJ, Baxter JD, Chiellini G, Scanlan TS, Dillmann WH. The Thyroid Hormone Receptor-β-Selective Agonist GC-1 Differentially Affects Plasma Lipids and Cardiac Activity. Endocrinology 2000 141:3057-64

Nosek TM, Brotto MAP, Essig DA, Mestril R, Conover RC, Dillmann WH, Kolbeck RC. Functional properties of skeletal muscle from transgenic animals with upregulated heat shock protein 70. Physiol Genomics 4:25-33, 2001.

Meyer M, Trost SU, Bluhm WF, Knot HJ, Swanson E, Dillmann WH. Impaired sarcoplasmic reticulum function leads contractile dysfunction and cardiac hypertrophy. Am J Physiol Heart Circ Physiol 280: H2046-H2052, 2001.

Lin KM, Lin B, Lian IY, Mestril R, Scheffler IE, Dillmann WH. Combined and individual mitochondrial Hsp60 and Hsp10 expression in cardiac myocytes protects mitochondrial function and prevents apoptotic cell deaths induced by simulated ischemia-reoxygenation. Circulation 103:1787-1792, 2001.

Gloss B, Trost SU, Bluhm WF, Swanson EA, Clark R, Winkfein R, Janzen KM, Giles W, Chassande O, Samarut J, Dillmann WH. Cardiac ion channel expression and contractile function in mice with deletion of thyroid hormone receptor α or β. Endocrinology 142:544-550, 2001.

Ray PS, Martin JL, Swanson EA, Otani H, Dillmann WH, Das DK. Transgene overexpression of αB crystallin confers simultaneous protection against cardiomyocyte apoptosis and necrosis during myocardial ischemia and reperfusion. FASEB J 15: 393-402, 2001.

Pascal G, Arness B Diaz S, Moore S, Patel T, Dillmann WH, Parekh R, Varki A. Proteomic comparison of human and great ape blood plasma reveals conserved glycosylation and differences in thyroid hormone metabolism. Am. J. Phys Anthropol 115:99-109, 2001.

Cummings CJ, Sun Y, Opal P, Antalffy B, Mestril R, Orr HT, Dillmann WH, Zoghbi HY: Over-expression of Inducible HSP70 Chaperone Suppresses Neuropathology and Improves Motor Function in SCA1 Mice. Human Molecular Genetics. 10(14): 1511-8, 2001.

Ito K, Yan X, Feng X, Manning WJ, Dillmann WH, Lorell BH: Transgenic expression of sarcoplasmic reticulum Ca(2+) ATPase modifies the transition from hypertrophy to early heart failure. Circ Res 89(5):422-9, 2001.

Baxter JD, Dillmann WH, West BL, Huber R, Furlow JD, Fletterick RJ, Webb P, Apriletti JW, Scanlan TS: Selective modulation of thyroid hormone receptor action. Journal of Steroid Biochemistry and Molecular Biology. 76(1-5):31-42, 2001.

Thuerauf DJ, Hoover H, Meller J, Hernandez, Su L, Andrews C, Dillmann WH, McDonough PM, Glembotski CC: Sarco/endoplasmic reticulum calcium ATPase-2 (SERCa2) expression is regulated by ATF6 during the endoplasmic reticulum stress response: Intracellular signaling of calcium stress in a cardiac myocyte model system. J Biol Chem 276: 48309-17, 2002.

Zhang T, Johnson EN, Gu Y, Morissette MR, Sah VP, Gigena MS, Belke DD, Dillmann WH, Rogers TB, Schulman H, Ross J Jr, Brown JH: The Cardiac-Specific Nuclear πB Isoform of Ca2+/Calmodulin-dependent protein kinase II induces hypertrophy and dilated cardiomyopathy associated with increased PP2A activity. J Biol Chem 277: 1261-67, 2002.

Cowling RT, Gurantz D, Peng J, Dillmann WH, Greenberg BH: Transcription factor NF –B is necessary for upregulation of type I angiotensin II receptor (AT1) mRNA in rat cardiac fibroblasts treated with TNFα or IL-1β. J Biol Chem. 2002;277(8):5719-5724.

Trost SU, Belke DD, Bluhm WF, Meyer M, Swanson E, Dillmann WH: Overexpression of the Sarcoplasmic Reticulum Ca2+ -ATPase Improves Myocardial Contractility in Diabetic Cardiomyopathy. Diabetes 2002;51:1-6.

II. INVITED ARTICLES:

Oppenheimer JH, Schwartz HL, Surks MI, Koerner DH, Dillmann WH: Physiological significance of nuclear receptor sites. In Thyroid Hormone Metabolism, Harland and Orr (eds), Academic Press, London, 1975.

Oppenheimer JH, Dillmann W: Molecular mechanisms at the tissue level in hyperthyroidism. Clinics in Endocrinology and Metabolism 1978; 17:145-165.

Oppenheimer JH, Dillmann WH: Nuclear receptors for triiodothyronine: A physiologic perspective In: Receptors and Hormone Action, L. Bimbaumer and B.W. O'Malley (eds), Academic Press, New York, 3:32, 1978.

Oppenheimer JH, Dillmann WH: Nuclear receptors in thyroid hormone action: A progress report. Fed. Proc. 1979; 38:2154-2161.

Towle HD, Dillmann WH, Schwartz HL, Oppenheimer JH: Interaction of thyroid hormones with target tissues: Effects on hepatic mRNA population. In Transmembrane Signaling, Alan R. Liss, Inc., New York, pp. 691-701, 1979.

Dillmann WH: Thyroid hormone and the heart. In: Thyroid Today, Vol. 2, No. 2, pp. 1-6, 1983.

Dillmann WH: Hormonal influences on cardiac myosin ATPase activity and myosin isoenzyme distribution. Mol. Cell. Endocrinol. 1984; 34:169-181.

Dillmann WH: Influence of thyroid hormone on messenger RNA levels in the rat heart. Plenary Lecture 7th International Congress of Endocrinology, Quebec, Canada, Elsevier Science Publishers B.V., July, 1984.

Dillmann WH: Mechanism of action of thyroid hormone. Medical Clinics of North America, Vol 69, No. 5, pp. 849-861, 1985.

Dillmann WH: Diabetes mellitus and hypothyroidism induces changes in myosin isoenzyme distribution in the rat heart - do alterations in fuel flux mediate these changes? In: Myocardial and Skeletal Muscle Bioenergetics, (Nachman Brautbar, eds) Plenum Publishing Corporation, pp. 469-479, 1986.

Dillmann WH, Rohrer D, Popovich B, Barrieux A: Thyroid hormone induced changes in cardiac proteins and mRNAs. In: Molecular Biological Approaches to Thyroid Research, Int'l Symposium Reiensburg, Georg Thieme Verlag Stuttgart Thieme Medical Publishers, Inc., New York, pp. 26-28, 1987.

Dillmann, WH: Diabetes mellitus-induced changes in the concentration of specific mRNAs and proteins. In: Diabetes/Metabolism Reviews, Vol. 4, No. 8, John Wiley & Sons, Inc., New York, pp. 789-797, 1988.

Dillmann WH, Rohrer D: The biochemical basis of hypothyroid heart disease. International MERCK-Symposium, Dusseldorf, Germany, 1988.

Dillmann, WH: Diabetes and thyroid-hormone-induced changes in cardiac function and their molecular basis. Ann. Rev. Med. 1989; 40:373-394.

Dillmann WH: Diabetes and thyroid-hormone-induced changes in cardiac function and their molecular basis. In: Annual Review of Medicine: Selected Topics in the Clinical Sciences, (W. P. Creger, C.H. Coggins, E.W. Hancock, eds), Annual Reviews, Inc., Palo Alto, CA,, Vol 40, pp. 373-394, 1989

Dillmann WH: Biochemical basis of thyroid hormone action in the heart. Amer. J. Med. 1990; 88:626-630.

Dillmann WH: Diabetes-induced changes in specific proteins and mRNAs in the rat heart. In: The Diabetic Heart, (eds by M. Nagano and N.S. Dhalla), Raven Press, Ltd., New York, pp. 263-270, 1991.

Dillmann WH: The cardiovascular system in hypothyroidism. In: Werner and Ingbar's The Thyroid, (L. Braverman and D. Utiger, eds), J.B. Lippincott Co., Philadelphia, PA, pp. 1002-1008, 1991.

Dillmann WH: The cardiovascular system in thyrotoxicosis. In: Werner and Ingbar's The Thyroid, (L. Braverman and D. Utiger, eds), J.B. Lippincott Co., Philadelphia, PA, pp. 759-770, 1991.

Mestril R, Dillmann WH: Heat shock and adaptive response to ischemia. Trends in Cardiovasc. Med. 1991; 1:240-244.

Mestril R, Dillmann WH: Heat shock proteins and protection against myocardial ischemia. J Mol Cell Cardiol 1995;27:45-52

Dillmann WH: Cardiac function in thyroid disease: Clinical features and management considerations. Annuals Thorac Surg 1993;56(1):S9-S15.

Dillmann WH, Mestril R: Heat shock proteins in myocardial stress. Zeitschrift fur Kardiologie 1995;84:87-90.

Mestril R, Dillmann WH. Heat shock proteins and protection against myocardial ischemia. J Mol Cell Cardiol 1995 27:45-52

Dillmann WH: Regulation of expression of cardiac sarcoplasmic reticulum proteins under pathophysiological conditions. Mol Cell Biochem 1996;157:125-128.

Dillmann WH: Thyroid hormones and the Heart: Basic mechanistic and clinical issues. Thyroid Today January/February/March 1996, pp 1-11.

Dillmann WH: Editorial: Thyroid Hormone Action and Cardiac Contractility - A Complex Affair. Endocrinology 1996;137:799-801.

Dillmann WH: The thyroid and its disorders. In: Cecil Textbook of Medicine, 20th Edition, (JC Bennett, F Plum, GN Gill, JP Kokko, GL Mandell, RK Ockner, TW Smith, eds), W.B. Saunders, New York, 1996, pp. 1227-1245.

Dillmann WH, Mestril R: Ischemia, Infarction and HSP70. In: Heat Shock Proteins and the Cardiovascular System, (Knowlton AA, eds), Kluwer Academic Publishers, Norwell, MA, pp.25-39, 1997.

Dillmann WH: Thyroid Storm. In: Current Therapy in Endocrinology and Metabolism, Sixth Edition, (Bardin CW, ed) Mosby-Year Book, Inc., Philadelphia, PA, pp. 81-85, 1997.

Meyer M, Dillmann WH: Sarcoplasmic reticulum Ca^{2+} -ATPase overexpression by adenovirus mediated gene transfer and transgenic mice. Cardiovascular Research 1998;37:360-366.

Dillmann WH: Influences of increased expression of the Ca^{2+}ATPase of the sarcoplasmic reticulum (SERCA2) by a transgenic approach on cardiac contractility. Ann. New York Acad Sci 1998:853:43-8.

Bluhm, WF; Meyer, M; Swanson, EA; Dillmann, WH. Postrest potentiation of active force in mouse papillary muscles is greatly accelerated by increased stimulus frequency. Annals of the New York Academy of Sciences, 1998:853:304-7.

Dillmann WH. Small heat shock proteins and protection against injury. Ann NY Acad Sci 1999 874:66-68

Dillmann WH. Heat shock proteins and protection against ischemic injury. Infect. Dis Obstet Gynecol 1999 7:55-57

Dillmann WH. Calcium regulatory proteins and their alteration by transgenic approaches. American Journal of Cardiology, 1999 83(12A):89H-91H

Dillmann WH: The Thyroid. In: Cecil Textbook of Medicine , 21st Edition W.B. Saunders Philadelphia, pp. 1231-1250, 2000.

Dillmann WH: Thyrotoxicosis and The Heart. In: Graves' Disease Pathogenesis and Treatment, Kluwer Academic Publishers Boston/Dordrecht/London, Chapter 16, pp. 227-234, 2000.